ENHANCED TRANSPORT USING MEMBRANE DISRUPTIVE AGENTS

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A61K47/32; A61K47/42; A61K47/48; A61K9/00

- European: A61K41/00M; A61K41/00T; A61K47/48T2

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Priority number(s): US19980070411P 19980105; WO1999US00122 19990105

Abstract not available for JP 2002500201 (T)

Abstract of corresponding document: WO 9934831 (A1)

Compositions and methods for transport or release of therapeutic and diagnostic agents or metabolites or other analytes from cells, compartments within cells, or through cell layers or barriers are described. The compositions include a membrane barrier transport enhancing agent and are usually administered in combination with an enhancer and/or exposure to stimuli to effect disruption or altered permeability, transport or release. In a preferred embodiment, the compositions include compounds which disrupt endosomal membranes in response to the low pH in the endosomes but which are relatively inactive toward cell membranes, coupled directly or indirectly to a therapeutic or diagnostic agent. Other disruptive agents can also be used, responsive to stimuli and/or enhancers other than pH, such as light, electrical stimuli, electromagnetic stimuli, ultrasound, temperature, or combinations thereof. The compounds can be coupled by ionic, covalent or H bonds to an agent to be delivered or to a ligand which forms a complex with the agent to be delivered. Agents to be delivered can be therapeutic and/or diagnostic agents. Treatments which enhance delivery such as ultrasound, iontopheresis, and/or electropheresis can also be used with the disrupting agents.

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Also published as:

🔼 WO9934831 (A1) EP1044021 (A1)

EP1044021 (B1) EP2138191 (A1) CA2317549 (A1)

more >>

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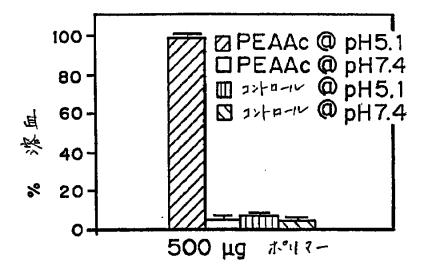
(74)代理人 弁理士 山本 秀策

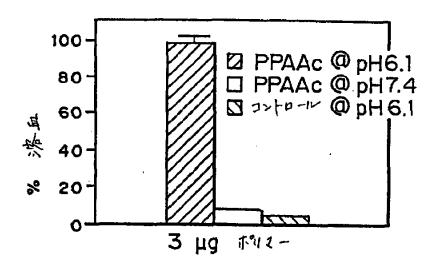
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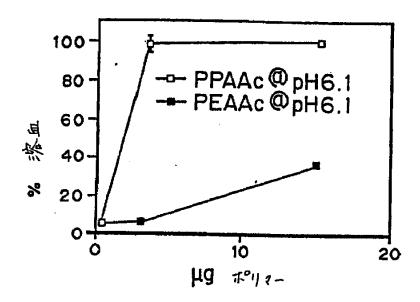
(54) 【発明の名称】 膜破壊剤を使用する増強された輸送

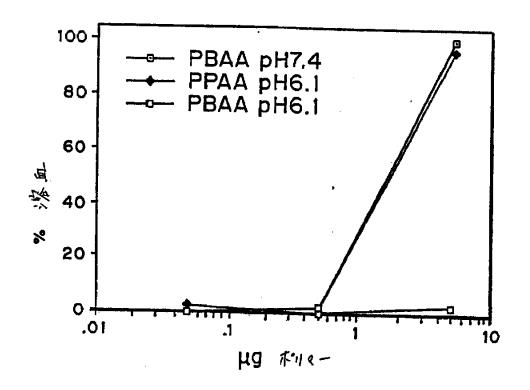
(57) 【要約】

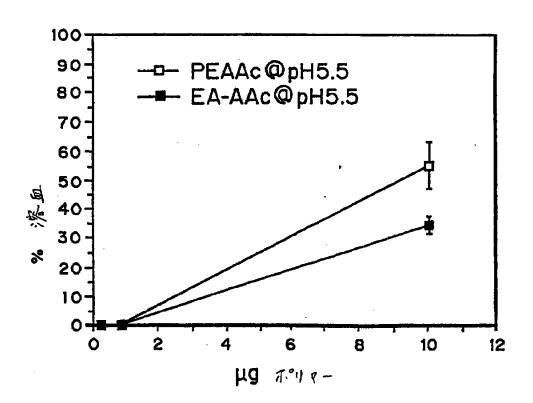
治療剤および診断剤、または代謝産物、または他の分析 物の、細胞からの、細胞内区画からの、あるいは細胞層 または細胞障壁を通っての、輸送あるいは放出のための 組成物および方法が記載される。これらの組成物は、膜 障壁輸送増強剤を含み、そして通常、増強因子および/ あるいは、破壊または透過性の変化、輸送の変化、もし くは放出の変化をもたらす刺激への曝露と組合せて投与 される。好ましい実施農様において、これらの組成物 は、エンドソームの低pHに応答してエンドソーム膜を 破壊するが、細胞膜に対しては比較的不活性である化合 物を含み、治療剤または診断剤と、直接あるいは間接的 に結合される。pH以外の刺激および/または増強因子 (例えば、光、電気的刺激、電磁気的刺激、超音波、温 度またはそれらの組合せ) に応答性である他の破壊剤も また使用され得る。これらの化合物は、イオン結合、共 有結合、または水素結合により、送達される薬剤あるい は送達される薬剤と複合体を形成するリガンドに結合さ れ得る。送達される薬剤は、治療剤および/または診断 剤であり得る。超音波、イオン泳動、および/または電 気泳動のような、送達を増強する処置もまた、破壊剤と 共に使用され得る。

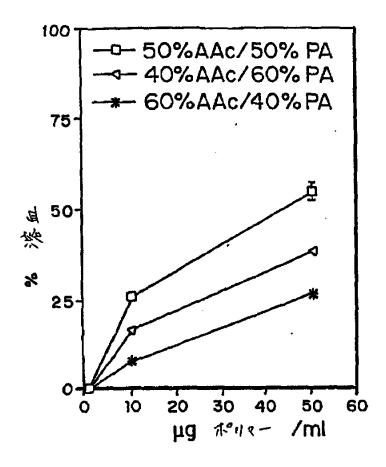


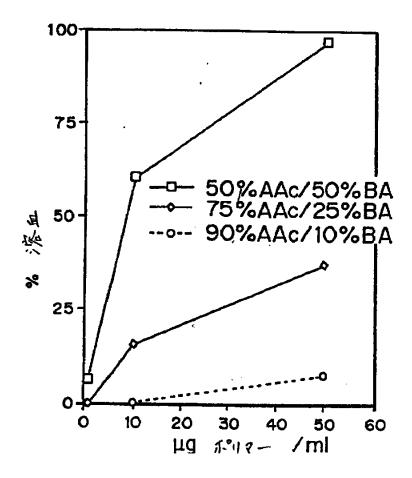


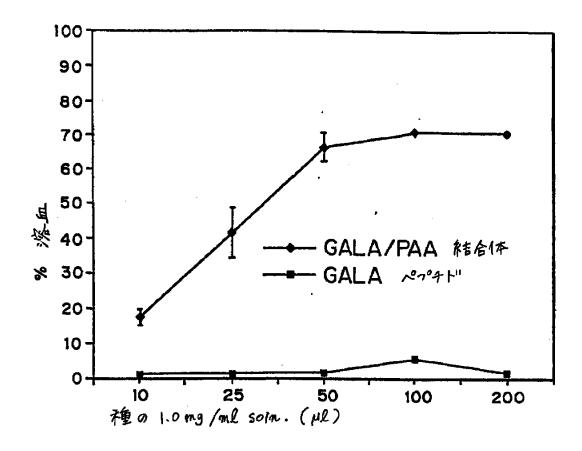


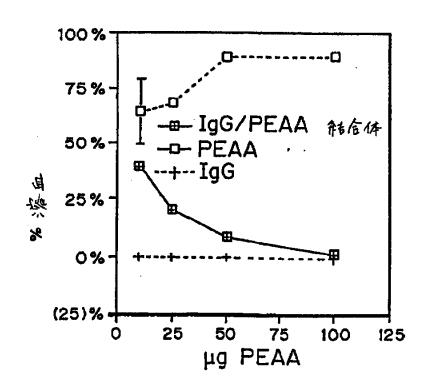


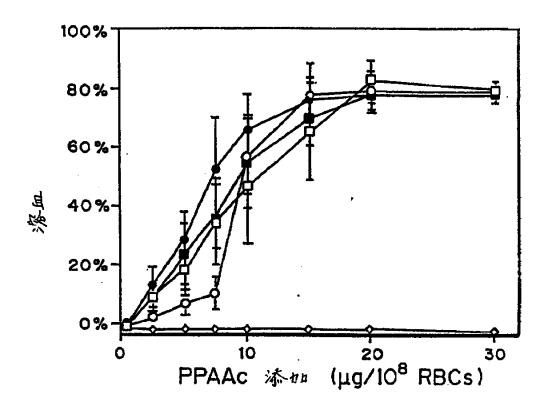


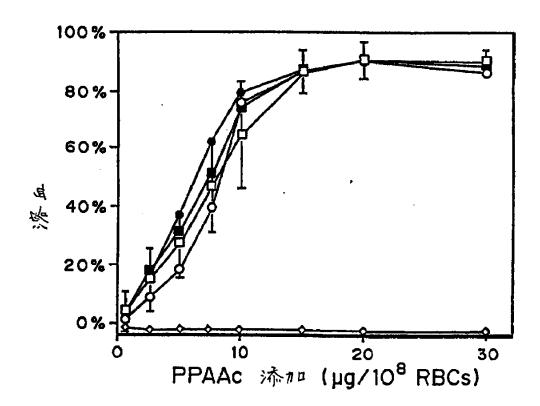


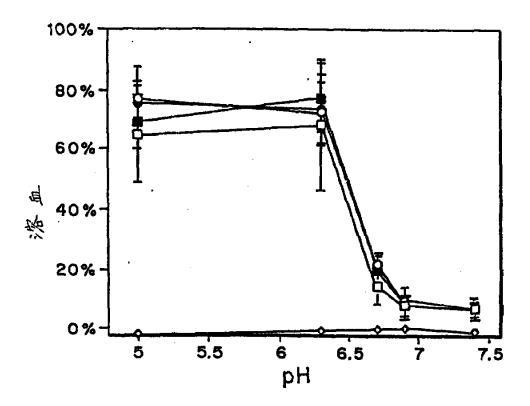


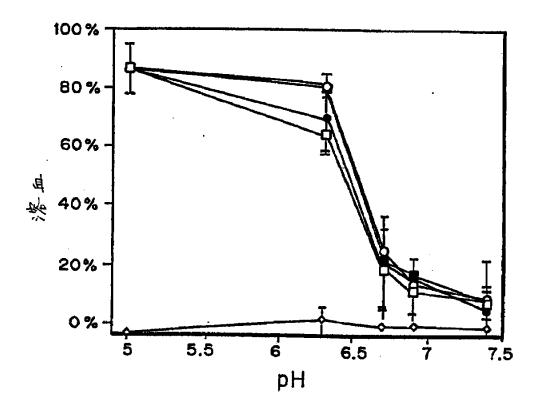


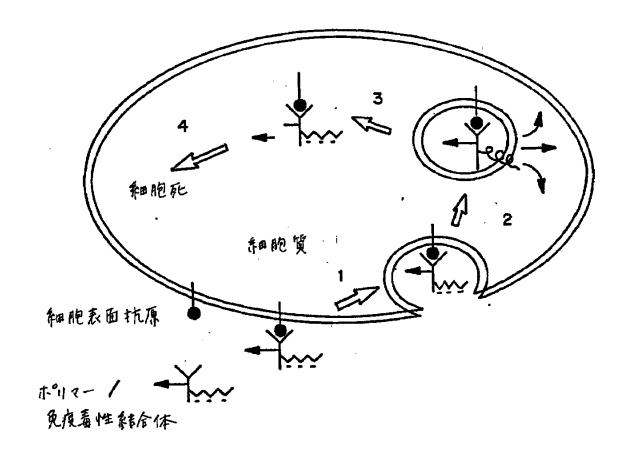


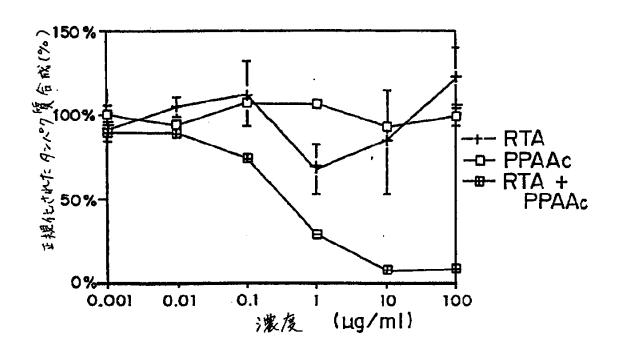




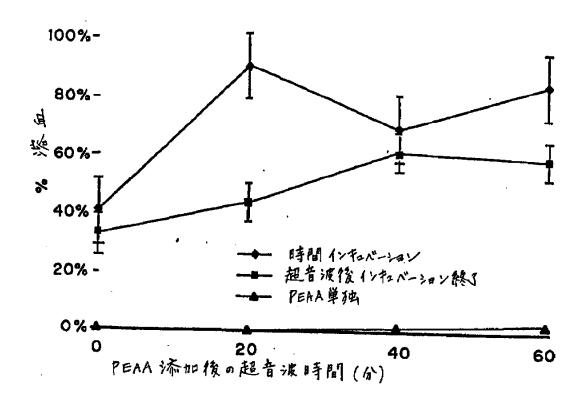


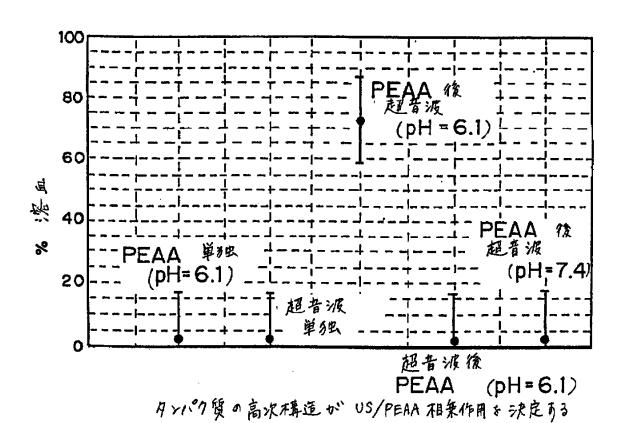












Inte Jonal Application No PCT/US 99/00122

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 A61K47/32 A61K47/42 A61K47/48 A61K41/00					
According	o International Patent Classification (IPC) or to both national classific	alice and IPC			
	SEARCHED	SINTERNITO			
	counentation searched (classification system followed by classification A61K	on symbols)			
Documenta	fion searched other than minimum documentation to the extent that s	uch documento are included in the fields so	earched		
Electionic	ata base consulted during the international search (name of data ba	se and, where practical search terms used	,		
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the ref	evant passeges	Refevant to claim No.		
X	WO 97 09068 A (UNIV WASHINGTON)	1-8,12			
A	13 March 1997 see page 4, line 11-20 see page 10, line 19 - page 22,]	15			
	see page 53, line 15 - page 54, l see claims see figure 8				
X	WO 96 40958 A (BAYLOR COLLEGE MED 19 December 1996	1,3,5,6, 8,11,12			
А	see page 7, line 7-24 see page 8, line 25-34 see page 9, line 34 - page 10, line 5-13 see page 13, line 5-13 see page 15, line 10-15 see page 19, line 21 - page 20, see page 66, line 18-22 see claims	15-20			
		-/			
X Fur	ther documents are listed in the continuation of box C.	X Patent family members are fisted	in annex.		
"A" document defining the general state of the left which is not considered to be of particular relevance. "E" saffer document but published on or after the international filling date or priority date and not in conflict with the application but ofted to understand the principle or theory underlying the invention of the gradient of the priority date and not in conflict with the application but ofted to understand the principle or theory underlying the invention of the gradient of the priority date and not in relevance; the claimed invention cannot be considered to involve an inventive slep when the document is taken alone "Y" document or particular relevance; the claimed invention cannot be considered to involve an inventive slep when the document is taken alone "Y" document or particular relevance; the claimed invention cannot be considered to involve an inventive slep when the document is taken alone inventive slep when the document is taken alone or document is combined with one or more other such document is combined with one or more other such document. "P" document published after the international filing date but light the priority date and not in conflict with the application but offed to understand the priority date and not in conflict with the application but offed to understand the priority date and not in conflict with the application but offed to understand the priority date and not in conflict with the application but offed to understand the priority date and not in conflict with the application but offed to understand the priority date and not in conflict with the application but offed to understand the priority date and not in the priority dat					
]	actual completion of the informational search	Date of mailing of the infernational set	arch report		
	meiting address of the ISA European Patent Office, P.B. 5818 Petentieen 2	Authorized officer			
	NL - 2280 HY Pljewijk Tel. (+31-70) 340-2049, Tx. 31 651 epc nl, Fax. (+31-70) 340-3016	La Gaetana, R			

Int tional Application No PCT/US 99/00122

2(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/US 99/00122
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	US 5 547 932 A (CURIEL DAVID T ET AL) 20 August 1996	1,3,5,6, 8,9,11, 12
A	see column 4, line 63 - column 5, line 29 see column 9, line 51-62 see column 15, line 36-51 see claims see example 12	15-20
х	PLANK C ET AL: "THE INFLUENCE OF ENDOSOME-DISRUPTIVE PEPTIDES ON GENE TRANSFER USING SYNTHETIC VIRUS-LIKE GENE TRANSFER SYSTEMS" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 17, 29 April 1994, pages 12918-12924, XP000615488 cited in the application see abstract see page 12918, column 1 see Disussion	1,3,5,6,
A	WO 97 04832 A (MASSACHUSETTS INST TECHNOLOGY) 13 February 1997 see page 6, line 1 - page 7, line 2 see page 11, line 10 - page 12, line 7 see page 12, line 34 - page 13, line 7 see page 23, line 21 - page 24, line 5 see claims 1,2,13,22-24	1-20
А	US 4 657 543 A (LANGER ROBERT S ET AL) 14 April 1987 see column 1, line 45-64 see column 4, line 41-61 see claims	1-20
x	HUGHES JA, ARONSHN AI, AVRUTSKAYA AV, JULIANO RL: "Evaluation of adjuvants that enhance the effectiveness of antisense oligodeoxynucleotides" PHARMACOLOGICAL RESEARCH, vol. 13, no. 3, March 1996, pages 404-10, KP002100198 cited in the application see abstract see Discussion	1,3,5,6, 12,13
A	KOST J, LANGER R: "Responsive poymer systems for controlled delivery of therapeutics" TRENDS INBIOTECHNOLOGY, vol. 10, no. 4, April 1992, pages 127-131, XP002100199 see the whole document	1~20

...ernational application No.
PCT/US 99/00122

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically: See FURTHER INFORMATION SHEET PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lecking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
As all searchable claims could be searched without effort justifying an additional lee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search feet were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Information on patent family members

Ints Ional Application No PCT/US 99/00122

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